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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,728	12/14/2005	Anders Kaplan	PU0359	3756

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EXAMINER	
XU, XIAOYUN	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,728	KAPLAN ET AL.	
	Examiner	Art Unit	
	ROBERT XU	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claim 23 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Computer program product is an abstract concept.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claim 19** is rejected under 35 U.S.C. 102(b) as being anticipated by Enke et al. (US Patent 5,175,430) (Enke).

In regard to claim 19, Enke discloses a measurement system for performing a combined Chromatography and Mass Spectrometry analysis on at least one sample for characterization of organic molecules species in the sample. The measurement system comprises chromatography column, a mass spectrometer interface, a mass spectrometer and means for control and analysis and the measurement system is adapted to:

perform an LC/MS analysis (see col. 5, lines 34-44);

generate elution profile, the elution profile being a multidimensional representations of the data resulting from the LC/MS analysis wherein one dimension is an elution time of the chromatography, and one dimension is mass to charge ratio (m/z), and one dimension a signal intensity (see col. 5, lines 49-53), and in which of the elution profile a characteristic any variation in the signal intensity is an indication of the existence of a specific organic molecule species (see col. 6, lines 16-23), and the signal from each molecule species is dispersed forming a plurality of signal peaks associated with each biomolecule species in the elution profile (see col. 5, line 59—col. 6, line 16, Figure 3-5, Col. 6, lines 34-37); and

reassemble the dispersed signal originating from one molecule species in the elution profile (see col. 6, line 38-41), and the measurement system is that reassembling methodology includes an automated annotation adapted to reassemble signal variations in the elution profile that originate from the same molecule species and generating a molecule map, said automated annotating being simultaneously based on at least both the elution time-dimension and the m/z-dimension (see col. 6, lines 42-53).

The system disclosed by Enke is capable of analyzing biomolecule species.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. **Claims 1, 2, 6-12, 17-18 and 24** are rejected under 35 U.S.C. 103(a) as being unpatentable over Enke et al. (US Patent 5,175,430) (Enke).

In regard to Claim 1, Enke teaches a method of performing a combined chromatography and mass spectrometry analysis on organic compounds in a sample. The method comprises the steps of:

performing a chromatography and mass spectrometry analysis (see col. 5, lines 34-44);

generating an elution profile, the elution profile has one dimension in elution time of the chromatography, and one dimension in mass to charge ratio (m/z), and one dimension in signal intensity (see col. 5, lines 49-53), the characteristic variation of the signal intensity is an indication of the existence of a specific species (see col. 6, lines 16-23), the signal from each species is dispersed forming a plurality of signal peaks in the elution profile (see col. 5, line 59—col. 6, line 16, Figure 3-5, Col. 6, lines 34-37);

reassembling the dispersed signal originating from one species in the elution profile (see col. 6, line 38-41); and the reassembling step includes an automated annotation to record signal variations in the elution profile that originate from the same

species and generating a 2-D map based on elution time-dimension and the m/z-dimension (see col. 6, lines 42-53).

Enke does not teach biomolecule species in the sample. Enke teaches organic molecule in the sample. Biomolecule species is an obvious variation of the organic molecule.

Enke teaches the 2-D profiling method for resolving organic compounds in time-compressed chromatography in mass spectrometry. Enke's method is equally useful in dealing with bimolecules having broad chromatography peaks in normal chromatography.

In regard to Claim 2, Enke teaches that the dispersion of signal from each organic compound arises from different isotope and/or charge (m/z) states, and the automated annotating reassembles the signal dispersion for essentially each compound caused by the different isotope and/or charge (m/z) states (see col. 7, lines 3-8).

In regard to Claims 6 and 7, Enke teaches using a priori assumptions of the relations between different charge and/or different isotope (m/z) states of the same molecule species in the reassembling of dispersed signals (see col. 6, line 64-68, col. 7, lines 1-8).

In regard to Claims 8 and 9, Enke teaches that the automated annotation in the reassembling is based on the fact that as a compound elutes from the chromatographic column, the intensities of all the m/z values contained in its mass spectrum will change synchronously, that is the intensity will remain in constant proportion to one another through the raise and fall in their value (see col. 6 lines 17-22). In other words, a first

signal pattern associated with a first charge state of a molecule species has a resemblance with a second signal pattern associated with a second charge state of the same molecule species. The assumption can be applied to isotope distribution associated molecule. The first isotope distribution associated with a first charge state of a molecule species has a resemblance with a second isotope distribution associated with a second charge state of the molecule species.

In regard to Claim 10, Enke teaches automated annotating. The annotating comprises the steps of:

a) finding and marking peaks in the signal variation of the elution profile (see col. 6, lines 38-41);

b) defining a first set of spots, wherein each spot including one primary feature and the spots have a variable extension in the m/z-dimension and a variable extension in the elution time dimension, and each spot is assumed to correspond to a specific charge state of a molecule (see col. 6 line 42-53);

c) constructing a molecule map entry for each spot by detecting a set of regions with a known structural relationship and confining the patterns from one species within the elution profile (see col. 6, lines 54-61); and

d) repeating steps (b) to (d) for each spot. An entry is created if for the charge state the structural relationships of the set of regions are essentially consistent and significant (see col. 7 lines 3-8, lines 23-25),

Enke does not specifically teach that an incomplete peptide map entry is created for the spot itself, if no charge state giving known structural relationship of the set of the

regions can be found. However, marking an incomplete entry for an inconclusive spot would have been an obvious option to a person of ordinary skill in the art.

In regard to Claims 11 and 12, Enke teaches determining peak positions in the individual ion chromatograms, generally by searching each ion chromatogram for the appearance of a peak (see col. 6, lines 38-41) and correlating the intensity of all the m/z values contained in ion chromatogram (see col.6, lines 16-22). That means for each putative charge z, the search will include detecting isotopes at m/z ±1/z, m/z ± 2/z, etc. or at (m-1)/(z±1)+1, (m-1)/(z±2)+1, etc., in order to confirm the entry of the molecule.

In regard to Claim 17, Enke teaches matching individual molecule maps generated in the reassembling step to form a global annotation (see col. 7, lines 17-40);

Enke also teaches reverse deconvolution algorithms for performing measurement and evaluation for profiling a relative abundance of some of the individual molecule species using the abundance profiles based on the global annotation obtained in the preceding steps (see col. 6, lines 62-68, col. 7 lines 1-16). Enke further teaches that the forward and reverse deconvolution can be combined in a various sequence for the analysis of data for a single sample (see col. 7 lines 17-40).

In regard to Claim 18, Enke does not teach defining subsets adapted for selecting subsets for further analysis. Defining subset of molecule species for further chromatography mass spectrometry analysis based on 2-D profiling is optimizing analytical conditions. It would have been obvious for ordinary skill in the art to optimize the analysis conditions based on the previous results.

In regard to Claim 24, Enke discloses computer program products stored on a computer for control an execution of the steps in Claim 1 (see col. 6, lines 16-68, col. 7, lines 1-40).

8. **Claims 3-5 and 13** are rejected under 35 U.S.C. 103(a) as being unpatentable over Enke in view of Gygi et al. (nature Biotechnology, 1999) (Gygi).

In regard to Claims 3-5, Enke does not teach chemical labeled and/or isotope labeled biomolecule. Gygi teaches using chemical labeled and/or isotope labeled biomolecule in mass spectrometry analysis. Gygi teaches that chemical labeled and isotope labeled biomolecule provides marker for identification and separation of signals. It would have been obvious to use chemical label and/or isotope label as taught by Gygi in Enke's method, in order to further disperse the peaks originating from a biomolecule in 2-D profiling analysis.

In regard to Claim 13, Enke does not teach detecting different label variants for each putative charge z. Gygi teaches using chemical labeled and/or isotope labeled biomolecule in mass spectrometry analysis. Gygi teaches that chemical labeled and isotope labeled biomolecule provides marker for identification and separation of signals. At the time of the invention it would have been obvious for a person of ordinary skill in the art to utilize the relations between label variants of the same bimolecules in mass spectrometry as taught by Gygi in Enke's method, because Gygi teaches that isotope labeled biomolecule provides marker for identification and separation of signals.

9. **Claims 14-16 and 20-22** are rejected under 35 U.S.C. 103(a) as being unpatentable over Enke in view of Yang et al. (Rapid Communications in mass spectrometry, 2002) (Yang).

In regard to Claims 14-16 and 20-22, Enke does not specifically teach constructing a 2-D profiling using different resolution modes based on the resolution characteristic of the mass spectrometer. Mass resolution R is the dimensionless ratio of the mass of the peak divided by its width. The mass resolution achievable by a mass spectrometer depends on both the type of analyzer and the experimental conditions. When molecular mass, m, is less than R, high resolution data of the molecular mass is achievable. Yang teaches mass spectrometer that is capable of acquiring low resolution (unit resolution) data and high resolution (enhanced resolution) data (see page 2062 right col. 1st and 2nd paragraph) and computer program for data acquisition and processing in low and high resolutions (see page 2062 right col. last paragraph). At time of the invention it would have been obvious for a person of ordinary skill in the art to use computer program to process data at both low and high resolution modes as taught by Yang in Enke 's method, so that both high resolution data and low resolution data can be processed.

Conclusion

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Brakstad (Chemometrics and intelligent laboratory systems, 1995) teaches method of extracting information from GC-MS using 2-D profiling.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

11/23/2008

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

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